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Letter to the Editor

Autism and Genetics: High Incidence of Specific Genetic Syndromes in 21 Autistic Adolescents and Adults Living in Two Residential Homes in Belgium

To the Editor:

In this journal, Hérault et al. [1995] reported a positive association between autism and two C-Harvey-ras (HRAS) oncogene markers in a study of 55 unrelated autistic children, mean age 7 years 4 months, and of 55 unrelated children, mean age 8 years 2 months, selected from a local normal school population. The authors reviewed the findings in several previous studies carried out concerning the role of genetic factors in autism and emphasized that some cases of autism have been associated with particular genetic disorders such as fragile X syndrome [Wahlström et al., 1986; Cohen et al., 1991; Tranebjaerg and Kure, 1991], tuberous sclerosis [Valente, 1971], phenylketonuria [Sorosky et al., 1968], and neurofibromatosis [Gillberg and Forsell, 1984].

Recently, we had the opportunity to examine a group of 21 adolescents and adults, 18 males and 3 females, aged between 16 and 32 years, with particular interest in the cause of their autistic or autism-spectrum behaviour.

All subjects stayed in "De Speling" and "Autigone," two residential group homes especially established for persons with autism or pervasive developmental disorders. At the time of the study, autistic disorder and pervasive developmental disorder was defined according to DSM-III-R criteria [APA, 1987]. Sixteen subjects received the diagnosis of autistic disorder (299.00), the remaining five subjects fulfilled the criteria for pervasive developmental disorder not otherwise specified (299.80). Family and personal histories of all individuals were obtained. Clinical examination with special attention for dysmorphic and neurological symptoms was done by the same clinical geneticist (JPF). High-resolution G-banded chromosome studies on peripheral blood-lymphocyte cultures and molecular studies of the FMR-1 mutation were performed in all individuals. If necessary for diagnosis, additional examination (ophthalmological, NMR brain scans and metabolic investigation) were performed. The subjects' mental level had been assessed by psychodiagnostic tests. Their mental level varied from normal intelligence to severe mental retardation: two persons had normal intelligence, one adolescent had a borderline IQ (IQ 71–85), three persons were mildly mentally retarded (IQ 55–70), twelve were moderately mentally retarded (IQ 35–54), and three severely mentally retarded (IQ 20–35). The three females were more severely retarded than the men: two moderately and one severely mentally retarded. In 13 of the 21 individuals (i.e., 61.9% of the patients) (see Table I) a precise etiological diagnosis could be made: a Mendelian inherited disorder in 12 individuals and a de novo autosomal reciprocal translocation [karyotype: 46,XY,t(1;15)(p35;q1233)] in one other. In 8/21 individuals no final etiological diagnosis was possible.

Gillberg and Coleman [1992] described 11 different syndromes which have a subgroup of affected individuals with an autistic syndrome: Cornelia de Lange syndrome, Fetal Alcohol syndrome, Hypomelanosis of Ito, Joubert syndrome, X-linked mental retardation with Marfanoid habitus (Lujan-Fryns syndrome), Moebius syndrome, Neurofibromatosis, Sotos syndrome, Gilles de la Tourette syndrome, Tuberous Sclerosis, and Williams-Beuren syndrome. The present study adds Shprintzen velocardiofacial syndrome (VCFS—MIM 192430), Noonan syndrome (MIM 216550), Basal cell nevus syndrome (MIM 109400), Adrenomyeloneuropathy (MIM 300100), Ceroid storage disease (MIM 214200), Peters' plus syndrome (MIM 261540), and de novo autosomal reciprocal translocation to this growing list. A remarkable finding in this study was also the diagnosis of X-linked mental retardation with Marfanoid habitus (MIM 309520) in four individuals and of Shprintzen VCFS (MIM 192430) in two individuals. Lalatta et al. [1991] and Fryns [1991] suggested that "psychotic behavior" may be a frequent manifestation in this X-linked mental retardation syndrome. The association of X-linked mental retardation with Marfanoid habitus and autism was confirmed by Gurrieri and Neri [1991]. Shprintzen VCFS [Shprintzen, 1978] is characterized by cleft palate or velopharyngeal insufficiency, cardiac anomalies, distinct facial appearance, learning disabilities, and/or mental retardation. A submicroscopic 22q11 deletion can be demonstrated by FISH in more than 80% of the patients [Scambler et al., 1992]. Besides the learning problems/mental retardation and the speech/language problems, a typical behavior profile and personality type has been reported: children with Shprintzen VCFS tend to have a bland affect with little facial expression; their social interaction seems to be different in terms of quantity

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TABLE I. Etiological Genetic Syndromic Diagnoses (N = 21)*

Diagnosis	Number
XLMR with Marfanoid habitus (MIM 309520)	4
Shprintzen velocardiofacial syndrome (MIM 192430)	2
Noonan syndrome (MIM 163950)	1
Cohen syndrome (MIM 216550)	1
Basal cell nevus syndrome (MIM 109400)	1
Adrenomyeloneuropathy (MIM 300100)	1
Ceroid storage disease (MIM 214200)	1
Peters' plus syndrome (MIM 261540)	1
46,XY,t(1;15)(p35;q1233)	1
Unknown	8

* MIM, Number in McKusick's catalog of Mendelian inheritance in man.

and quality [Golding-Kusher et al., 1985]. Shprintzen et al. [1992] stressed the need for follow-up of patients with VCFS. In at least 10% of the patients, they observed "schizophrenia-like," symptoms including psychosis which becomes evident with age.

Although family and twin studies have shown that hereditary factors play a role in autism, suggesting the existence of a still unknown gene, clinicians should not only rely on these epidemiological findings. The results of the present study, performed on a relatively small number of autistic individuals, indicates the importance of and the need for a thorough medical and clinical genetic evaluation in all children and adults with autism or autism-spectrum disorders.

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